

Atty. Dkt. No. 034536-0688

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants: Gregory PLOWMAN et al.  
Title: PAK5 SCREENING METHODS  
Appl. No.: 10/725,329  
Filing Date: 12/02/2003  
Examiner: Unassigned  
Art Unit: 1652

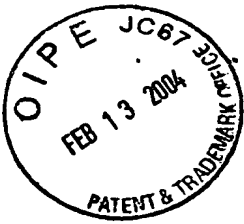
**INFORMATION DISCLOSURE STATEMENT**  
**UNDER 37 CFR §1.56**

Mail Stop PATENT APPLICATION  
Commissioner for Patents  
PO Box 1450  
Alexandria, Virginia 22313-1450

Sir:

Applicants submit herewith on Form PTO/SB/08 a listing of the documents cited by or submitted to the U.S. PTO in parent application Serial No. 09/688,188, filed 10/16/2000. As provided in 37 CFR §1.98(d), copies of the documents are not being provided since they were previously submitted to the United States Patent & Trademark Office in the above-identified parent application.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.



**TIMING OF THE DISCLOSURE**

The listed documents are being submitted in compliance with 37 CFR §1.97(b), within three (3) months of the filing date of the application.

**RELEVANCE OF EACH DOCUMENT**

The relevance of the listed documents is explained in the parent application.

Applicants respectfully request that any listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 CFR §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Respectfully submitted,

Date 2/13/04

FOLEY & LARDNER

Customer Number: 22428

Telephone: (202) 672-5475

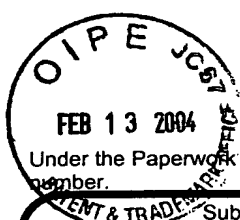
Facsimile: (202) 672-5399

By Beth A. Burrous

Beth A. Burrous

Attorney for Applicants

Registration No. 35,087



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

Date Submitted: February 13, 2004

(use as many sheets as necessary)

Sheet 1 of 15

**Complete if Known**

|                        |                 |
|------------------------|-----------------|
| Application Number     | Unassigned      |
| Filing Date            | 12/02/2003      |
| First Named Inventor   | Gregory Plowman |
| Group Art Unit         | 1652            |
| Examiner Name          | Unassigned      |
| Attorney Docket Number | 034536-0688     |

**U.S. PATENT DOCUMENTS**

| Examiner Initials* | Cite No. <sup>1</sup> | U.S. Patent Document |                                   | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
|--------------------|-----------------------|----------------------|-----------------------------------|---|--|---|
|                    |                       | Number               | Kind Code <sup>2</sup> (if known) |   |  |   |
|                    | A1                    | 4,343,940            |                                   | Kreighbaum                                      | 08/10/1982                                       |   |
|                    | A2                    | 4,376,110            |                                   | David et al.                                    | 03/08/1983                                       |   |
|                    | A3                    | 4,447,608            |                                   | Jones   | 05/08/1984                                       |   |
|                    | A4                    | 4,757,072            |                                   | Kabbe   | 07/12/1988                                       |   |
|                    | A5                    | 4,945,050            |                                   | Sanford   | 07/31/1990                                       |   |
|                    | A6                    | 5,217,999            |                                   | Levitzki  | 06/08/1993                                       |   |
|                    | A7                    | 5,302,606            |                                   | Spada   | 04/12/1994                                       |   |
|                    | A8                    | 5,316,553            |                                   | Kaul  | 05/31/1994                                       |   |
|                    | A9                    | 5,330,992            |                                   | Eissenstat                                      | 07/19/1994                                       |   |
|                    | A10                   | 6,013,500            |                                   | Minden  | 01/2000  |   |

**FOREIGN PATENT DOCUMENTS**

| Examiner Initials* | Cite No. <sup>1</sup> | Foreign Patent Document |                      |                                   | Name of Patentee or Applicant of Cited Documents | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T <sup>6</sup> |
|--------------------|-----------------------|-------------------------|----------------------|-----------------------------------|--|--|---|----------------|
|                    |                       | Office <sup>3</sup>     | Num ber <sup>4</sup> | Kind Code <sup>5</sup> (if known) |  |  |   |                |
|                    | A11                   | WO                      | 91/15495             |                                   | Dow  | 10/17/1991                                       |   |                |
|                    | A12                   | EP                      | 0 520 722            | A1                                | Barker   | 06/22/1992                                       |   |                |
|                    | A13                   | PCT                     | 92/21660             |                                   | Dow  | 12/10/1992                                       |   |                |
|                    | A14                   | PCT                     | 92/20642             |                                   | Spada  | 11/26/1992                                       |   |                |
|                    | A15                   | PCT                     | 93/09236             |                                   | Schwartz   | 05/13/1993                                       |   |                |
|                    | A16                   | EPO                     | 0 562 734            | A1                                | Pegg   | 09/29/1993                                       |   |                |
|                    | A17                   | EPO                     | 0 566 226            | A1                                | Barker   | 10/20/1993                                       |   |                |
|                    | A18                   | WO                      | 94/03427             |                                   | Dobrusin   | 02/17/1994                                       |   |                |
|                    | A19                   | WO                      | 94/14808             |                                   | Buzetti  | 07/07/1994                                       |   |                |
|                    | A20                   | WO                      | 96/22976             |                                   | Buzzetti   | 08/01/1996                                       |   |                |
|                    | A21                   | WO                      | 97 42212             |                                   |  | 11/13/1997                                       |   |                |
|                    | A22                   | WO                      | 99 15635             |                                   |  | 04/01/1999                                       |   |                |
|                    | A23                   | WO                      | 99 32637             |                                   |  | 07/01/1999                                       |   |                |
|                    | A24                   | WO                      | 99 07854             |                                   |  | 02/18/1999                                       |   |                |
|                    | A25                   | WO                      | 99 02699             |                                   |  | 01/21/1999                                       |   |                |

**NON PATENT LITERATURE DOCUMENTS**

| Examiner Initials* | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>6</sup> |
|--------------------|-----------------------|--|----------------|
|                    | A26                   | Abe et al., "Molecular Characterization of a Novel Metabotropic Glutamate Receptor mGluR5 Coupled to Inositol Phosphate/Ca <sup>2+</sup> Signal," J. Biol. Chem. 267(19):13361-13368 (1992)  |                |

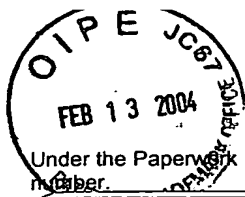
Examiner  
SignatureDate  
Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.



MODIFIED PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

|  |   |    |    |                               |                 |
|--|---|----|----|-------------------------------|-----------------|
| Substitute for form 1449B/PTO  |   |    |    | <b>Complete if Known</b>      |                 |
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br>Date Submitted: February 13, 2004<br><br>(use as many sheets as necessary) |   |    |    | <b>Application Number</b>     | Unassigned      |
|  |   |    |    | <b>Filing Date</b>            | 12/02/2003      |
|  |   |    |    | <b>First Named Inventor</b>   | Gregory Plowman |
|  |   |    |    | <b>Group Art Unit</b>         | 1652            |
|  |   |    |    | <b>Examiner Name</b>          | Unassigned      |
| <b>Sheet</b>   | 2 | of | 15 | <b>Attorney Docket Number</b> | 034536-0688     |

| NON PATENT LITERATURE DOCUMENTS |                       |  |  |                |
|---------------------------------|-----------------------|--|--|----------------|
| Examiner Initials*              | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. |  | T <sup>6</sup> |
|                                 | A27                   | ABO et al., "PAK4, A Novel Effector For Cdc42Hs, Is Implicated In The Reorganization Of The Actin Cytoskeleton And In The Formation Of Filopodia", The EMBP Journal, Vol. 17, No. 22, Pages 6527-6540, 16 November 1998  |  |                |
|                                 | A28                   | Allen et al., "Modulation of CD4 by suramin," <u>Clin. Exp. Immunol.</u> 91:141-146 (1991)   |  |                |
|                                 | A29                   | Allen et al., "PAK3 Mutation in Nonsyndromic X-linked Mental Retardation," <u>Nat. Genet.</u> 20:25-30 (1998)  |  |                |
|                                 | A30                   | Altschul et al., "Gapped BLAST and PSI-BLAST: A New Generation of Protein Database Search Programs," <u>Nucleic Acids Research</u> 25:3389-3402 (1997)   |  |                |
|                                 | A31                   | Altschul et al., "Basic Local Alignment Search Tool," <u>J. Mol. Biol.</u> 215:403-410 (1990)  |  |                |
|                                 | A32                   | Anafi et al., "SH2/SH3 Adaptor Proteins Can Link Tyrosine Kinases to a Ste20-Related Protein Kinase, HPK1*," <u>J. Biol. Chem.</u> 272:27804-27811 (1997)  |  |                |
|                                 | A33                   | Anafi et al., "Tyrphostin-Induced Inhibition of p210 <sup>bcr-abl</sup> Tyrosine Kinase Activity Induces K562 to Differentiate," <u>Blood</u> 82:3524-3529 (1993)  |  |                |
|                                 | A34                   | Andrews et al. (American Veterinary Medicine Association Panel on Euthanasia), "1993 Report of the AVMA Panel on Euthanasia," <u>J. American Veterinary Medicine Association</u> 202(2):229-249 (1993)   |  |                |
|                                 | A35                   | Bagrodia et al., "Identification of a Mouse p21Cdc42/Rac Activated Kinase," <u>J. Biol. Chem.</u> 270:22731-22737 (1995)   |  |                |
|                                 | A36                   | Baker et al., "Induction of acetylcholine receptor clustering by native polystyrene beads," <u>Journal of Cell Science</u> 102:543-555 (1992)  |  |                |
|                                 | A37                   | Barker et al., "In vitro activity of non-glutamate containing quinazoline-based thymidylate synthase inhibitors," <u>Proceedings of the American Association for Cancer Research</u> 32:327 at abstract no. 1939 (1991)  |  |                |
|                                 | A38                   | Bayer et al., "The Avidin-Biotin Complex in Affinity Cytochemistry," <u>Methods in Enzymology</u> 62:308-319 (1979)  |  |                |
|                                 | A39                   | Benoist and Chambon, "In vivo sequence requirements of the SV40 early promoter region," <u>Nature</u> 290:304-310 (1981)   |  |                |
|                                 | A40                   | Berger and Wahl, "Screening Colonies or Plaques with Radioactive Nucleic Acid Probes," <u>Meth. Enzym.</u> 152:421 (1987)  |  |                |

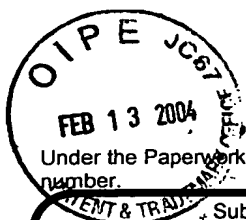
|                           |  |                        |  |
|---------------------------|--|------------------------|--|
| <b>Examiner Signature</b> |  | <b>Date Considered</b> |  |
|---------------------------|--|------------------------|--|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

|  |   |                               |                 |
|--|---|-------------------------------|-----------------|
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br>Date Submitted: February 13, 2004<br><br>(use as many sheets as necessary) |   | <b>Complete if Known</b>      |                 |
|  |   | <b>Application Number</b>     | Unassigned      |
|  |   | <b>Filing Date</b>            | 12/02/2003      |
|  |   | <b>First Named Inventor</b>   | Gregory Plowman |
|  |   | <b>Group Art Unit</b>         | 1652            |
|  |   | <b>Examiner Name</b>          | Unassigned      |
| <b>Sheet</b>   | 3 | <b>of</b>                     | 15              |
|  |   | <b>Attorney Docket Number</b> | 034536-0688     |

| NON PATENT LITERATURE DOCUMENTS |                       |  |                |
|---------------------------------|-----------------------|--|----------------|
| *Examiner Initials*             | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>6</sup> |
|                                 | A41                   | Bertino, "Toward Improved Selectivity in Cancer Chemotherapy: The Richard and Hinda Rosenthal Foundation Award Lecture," <u>Cancer Research</u> 39:293-304 (1979)  |                |
|                                 | A42                   | Bilder et al., "Tyrphostins inhibit PDGF-induced DNA synthesis and associated early events in smooth muscle cells," <u>Am. J. Physiol.</u> 260(Cell Physiol.29):C721-C730 (1991)   |                |
|                                 | A43                   | Bollon and Stauver, "DNA Transformation Efficiency of Various Bacterial and Yeast Host-Vector Systems," <u>Journal of Clinical Hematology and Oncology</u> 10(2&3):39-48 (1980)  |                |
|                                 | A44                   | Botstein et al., "Making Mutations in vitro and Putting Them Back into Yeast," <u>Miami Winter Symposia - From Gene to Protein: Translation into Biotechnology</u> , edited by Ahmad et al., Academic Press, 19:265-274 (1982)                                 |                |
|                                 | A45                   | Brinster et al., "Factors Affecting the Efficiency of Introducing Foreign DNA into Mice by Microinjecting Eggs," <u>Proc. Natl. Acad. Sci. USA</u> 82:4438-4442 (1985)   |                |
|                                 | A46                   | Broach, "The Yeast Plasmid 2 $\mu$ Circle," <u>Cell</u> 28:203-204 (1982)  |                |
|                                 | A47                   | Broach, "The Yeast Plasmid 2 $\mu$ Circle," in <u>The Molecular Biology of the Yeast Saccharomyces: Life Cycle and Inheritance</u> , Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, pp. 445-470 (1981)   |                |
|                                 | A48                   | Brown et al., "Human Ste20 Homologue hPAK1 Links GTPases to the JNK MAP Kinase Pathway," <u>Current Biol.</u> 6:598-605 (1996)   |                |
|                                 | A49                   | Brunton et al., "Anti-tumour activity of novel tryphostins in breast cancer cells," <u>Proceedings of the American Association for Cancer Research</u> 33:558 at abstract no. 3335 (1992)  |                |
|                                 | A50                   | Bryckaert et al., "Inhibition of Platelet-Derived Growth Factor-Induced Mitogenesis and Tyrosine Kinase Activity in Cultured Bone Marrow Fibroblasts by Tyrphostins," <u>Exp. Cell Research</u> 199:255-261 (1992)   |                |
|                                 | A51                   | Buccione et al., "The Acceleration of Anterograde Membrane Traffic is an Immediate Event Following the Activation of Multiple Plasmms Membrane Receptors," <u>Mol. Bio. Cell</u> 6:291 (1995)  |                |
|                                 | A52                   | Bucher et al., "A Flexible Motif Search Technique Based On Generalized Profiles", Computers And Chemistry, Gb, Pergamon Press, Oxford, Vol. 20, No. 1, Pages 3-23, 1996  |                |
|                                 | A53                   | Bullock and Petrusz (eds.), <u>Techniques in Immunocytochemistry</u> , Academic Press, Orlando, FL: Vol. 1 (1982), Vol. 2 (1983), Vol. 3 (1985) (TABLE OF CONTENTS ONLY)   |                |
|                                 | A54                   | Burbelo et al., "A Conserved Binding Motif Defines Numerous Candidate Target Proteins for Both Cdc42 and Rac GTPases," <u>J. Biol. Chem.</u> 270:29071-290740 (1995)   |                |

Examiner  
Signature

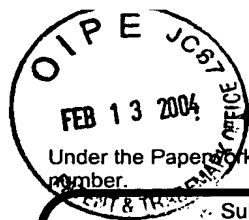
Date  
Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

MODIFIED PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

|  |  |                          |                 |
|--|--|--------------------------|-----------------|
| <b>Substitute for form 1449B/PTO</b><br><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b><br>Date Submitted: February 13, 2004<br>(use as many sheets as necessary) |  | <b>Complete if Known</b> |                 |
|  |  | Application Number       | Unassigned      |
| Sheet 4 of 15  |  | Filing Date              | 12/02/2003      |
|  |  | First Named Inventor     | Gregory Plowman |
|  |  | Group Art Unit           | 1652            |
|  |  | Examiner Name            | Unassigned      |
|  |  | Attorney Docket Number   | 034536-0688     |

| NON PATENT LITERATURE DOCUMENTS |                       |  |                |
|---------------------------------|-----------------------|--|----------------|
| Examiner Initials*              | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>6</sup> |
|                                 | A55                   | Burke et al., "Arylamides of Hydroxylated Isoquinolines as Protein-Tyrosine Kinase Inhibitors," <u>Bioorganic &amp; Medical Chemistry Letters</u> 2(12):1771-1774 (1992)   |                |
|                                 | A56                   | Burke et al., "Bicyclic Compounds as Ring-Constrained Inhibitors of Protein-Tyrosine Kinase p56 <sup>lck</sup> ," <u>Journal of Medicinal Chemistry</u> 36(4):425-432 (1993)   |                |
|                                 | A57                   | Campbell, <u>Monoclonal Antibody Technology: Laboratory Techniques in Biochemistry and Molecular Biology</u> , Volume 13, Elsevier Science Publishers, Amsterdam, The Netherlands (1984) (TABLE OF CONTENTS ONLY)  |                |
|                                 | A58                   | Capecchi, "Altering the Genome by Homologous Recombination," <u>Science</u> 244:1288-1292 (1989)   |                |
|                                 | A59                   | Capecchi, "High Efficiency Transformation by Direct Microinjection of DNA into Cultured Mammalian Cells," <u>Cell</u> 22:479-488 (1980)  |                |
|                                 | A60                   | Cenatiempo, "Prokaryotic gene expression in vitro: transcription-translation coupled systems," <u>Biochimie</u> 68:505-515 (1986)  |                |
|                                 | A61                   | Chard, <u>An Introduction to Radioimmunoassay and Related Techniques</u> , Elsevier Science Publishers, Amsterdam, The Netherlands (1986) (TABLE OF CONTENTS ONLY)   |                |
|                                 | A62                   | Chater et al., "Streptomyces ØC31-Like Phages: Cloning Vectors, Genome Changes and Host Range," in <u>Sixth International Symposium on Actinomycetes Biology</u> , edited by Szabe et al., Akademiai Kiado, Budapest, Hungary, pp. 45-52 (1986)                |                |
|                                 | A63                   | Chen and Okayama, "High-Efficiency Transformation of Mammalian Cells by Plasmid DNA," <u>Molecular and Cellular Biology</u> 7(8):2745-2752 (1987)  |                |
|                                 | A64                   | Chomczynski and Sacchi, "Single-Step Method of RNA Isolation by Acid Guanidinium Thiocyanate-Phenol-Chloroform Extraction," <u>Analytical Biochemistry</u> 162:156-159 (1987)  |                |
|                                 | A65                   | Chu et al., "Electroporation for the efficient transfection of mammalian cells with DNA," <u>Nucleic Acids Research</u> 15:1311-1326 (1987)  |                |
|                                 | A66                   | Cullen, "HIV-1: Is Nef a PAK Animal?" <u>Curr. Biol.</u> 6:1557-1559 (1996)  |                |
|                                 | A67                   | Curiel et al., "Gene Transfer to Respiratory Epithelial Cells via the Receptor-mediated Endocytosis Pathway," <u>Am. J. Respir. Cell. Mol. Biol.</u> 6:247-252 (1992)  |                |
|                                 | A68                   | Curtin et al., "Inhibition of the growth of human hepatocellular carcinoma in vitro and in athymic mice by a quinazoline inhibitor of thymidylate synthase, CB3717," <u>Br. J. Cancer</u> 53:361-368 (1986)  |                |

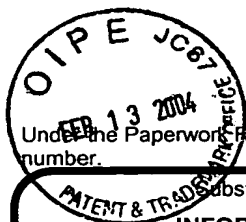
|                    |  |                 |  |
|--------------------|--|-----------------|--|
| Examiner Signature |  | Date Considered |  |
|--------------------|--|-----------------|--|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.



MODIFIED PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

|   |   |                          |                 |
|---|---|--------------------------|-----------------|
| Substitute for form 1449B/PTO<br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>Date Submitted: February 13, 2004<br>(use as many sheets as necessary) |   | <b>Complete if Known</b> |                 |
|   |   | Application Number       | Unassigned      |
|   |   | Filing Date              | 12/02/2003      |
|   |   | First Named Inventor     | Gregory Plowman |
|   |   | Group Art Unit           | 1652            |
|   |   | Examiner Name            | Unassigned      |
| Sheet   | 5 | of                       | 15              |
|   |   | Attorney Docket Number   | 034536-0688     |

| NON PATENT LITERATURE DOCUMENTS |                       |  |                |
|---------------------------------|-----------------------|--|----------------|
| Examiner Initials*              | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>6</sup> |
|                                 | A69                   | Daniels et al., "Membrane Targeting of p21-Activated Kinase 1 (PAK1) Induces Neurite Outgrowth from PC12 Cells," <u>EMBO J.</u> 17:754-764 (1998)  |                |
|                                 | A70                   | Database EMBL [Online], ID: AA576724, NCI-CGAP: "...Homo Sapiens cDNA Clone IMAGE:1074607", 11 September 1997  |                |
|                                 | A71                   | Database EMBL [Online], ID: AA634299, Hillier et al., "...Homo Sapiens cDNA Clone 743770 3' ", 31 October 1997   |                |
|                                 | A72                   | Database EMBL [Online], ID: AA766905, NCI-CGAP: "...Homo Sapiens cDNA Clone Image:1301771 Similar To TR:Q42341 Q42341 Serine-Threonine Protein Kinase...", 30 January 1998   |                |
|                                 | A73                   | Database EMBL [Online], ID: AA865818, NCI-CGAP: "...Homo Sapiens cDNA Clone IMAGE:1456752 3' Similar To TR:P97820 P97820NIK...", 16 March 1998   |                |
|                                 | A74                   | Database EMBL [Online], ID: AA885355, NCI-CGAP: "...Homo Sapiens cDNA Clone IMAGE:1460315 3' Similar To WP:T17E9.1 CE01405", 30 March 1998   |                |
|                                 | A75                   | Database EMBL [Online], ID: AB011123, Ohara et al., "Homo Sapiens mRNA For KIAA0551 Protein, Partial CDs", 10 April 1998   |                |
|                                 | A76                   | Database EMBL [Online], ID: AB015718, Kuramochi et al., "Homo Sapiens LOK mRNA For Protein Kinase, Complete CDs", 14 December 1998   |                |
|                                 | A77                   | Database EMBL [Online], ID: AF017635, Baytel et al., "Homo Sapiens DCHT mRNA, Complete CDs", 23 September 1997   |                |
|                                 | A78                   | Database EMBL [Online], ID: AF099989, Johnston et al., "SPAK: A Novel Ste-20 Related Kinase Expressed In The Pancreas", 11 November 1998   |                |
|                                 | A79                   | Database EMBL [Online], ID: HS1254308, , NCI-CGAP: "...Homo Sapiens cDNA Clone IMAGE:814858 5' Similar To WP:T19A5.2 CE07510 Serine. Threonine Kinase", 16 June 1997   |                |
|                                 | A80                   | Database EMBL [Online], ID: HS1254577, Hillier et al., "...Homo Sapiens cDNA Clone 796310 5' Similar To WP:ZC504.4 CE02384 Serine/Threonine Protein Kinase", 13 June 1997  |                |
|                                 | A81                   | Database EMBL [Online], ID: HS1259479, NCI-CGAP: "...Homo Sapiens cDNA Clone IMAGE:814858 3' Similar To TR:G881958 G881958 MESS1", 20 June 1997  |                |
|                                 | A82                   | Database EMBL [Online], ID: HS130B11B, Fujiwara et al., "Human Fetal Brain cDNA 5' -end GEN-130B11", 25 August 1995  |                |

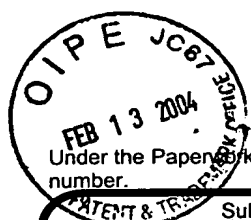
|                    |  |                 |  |
|--------------------|--|-----------------|--|
| Examiner Signature |  | Date Considered |  |
|--------------------|--|-----------------|--|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

MODIFIED PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

|   |   |                          |                 |
|---|---|--------------------------|-----------------|
| Substitute for form 1449B/PTO<br><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b><br>Date Submitted: February 13, 2004<br>(use as many sheets as necessary) |   | <b>Complete if Known</b> |                 |
|   |   | Application Number       | Unassigned      |
|   |   | Filing Date              | 12/02/2003      |
|   |   | First Named Inventor     | Gregory Plowman |
|   |   | Group Art Unit           | 1652            |
|   |   | Examiner Name            | Unassigned      |
| Sheet   | 6 | of                       | 15              |
|   |   | Attorney Docket Number   | 034536-0688     |

| NON PATENT LITERATURE DOCUMENTS |                       |  |                |
|---------------------------------|-----------------------|--|----------------|
| Examiner Initials*              | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>6</sup> |
|                                 | A83                   | Database EMBL [Online], ID: HS571200, Hillier et al., "yr32h1l.r Homo Sapiens cDNA Clone 207045 5' ", 15 September 1995  |                |
|                                 | A84                   | Database EMBL [Online], ID: MM1266197, Marra et al., "...Mus Musculus cDNA Clone 805425 5' Similar To WP:T17E9.1 CE01405", 22 June 1997  |                |
|                                 | A85                   | Database EMBL [Online], ID: MMAA20708, Marra et al., "mp54a01.r Soares 2NbMT Mus Musculus cDNA Clone 573000 5' ", 21 November 1996   |                |
|                                 | A86                   | Diener et al., "Activation Of The c-Jun N-terminal Kinase Pathway By A Novel Protein Kinase Related To Human Germinal Center Kinase", Proc. Natl. Acad. Sci. USA, Vol 94, Pages 9687-9692, September 1997  |                |
|                                 | A87                   | Dolle et al., "5,7-Dimethoxy-3-(4-pyridinyl)quinoline is a Potent and Selective Inhibitor of Human Vascular $\beta$ -Type Platelet-Derived Growth Factor Receptor Tyrosine Kinase," J. Med. Chem. 37:2627-2629 (1994)  |                |
|                                 | A88                   | Dong et al., "Activation of tumoricidal properties in macrophages by lipopolysaccharide requires protein-tyrosine kinase activity," Journal of Leukocyte Biology 53:53-60 (1993)   |                |
|                                 | A89                   | Dong et al., "Protein Tyrosine Kinase Inhibitors Decrease Induction of Nitric Oxide Synthase Activity in Lipopolysaccharide-Responsive and Lipopolysaccharide-Nonresponsive Murine Macrophages," The Journal of Immunology 151(5):2717-2724 (1993)             |                |
|                                 | A90                   | Dreborg et al., "Ch. 10 - The chemistry and standardization of allergens," in Handbook of Experimental Immunology - Volume 1: Immunochemistry, 4th Ed., edited by Weir et al., Blackwell Scientific Publications, Oxford, England, pp. 10.1 - 10.28 (1986)     |                |
|                                 | A91                   | Engvall and Perlmann, "Enzyme-Linked Immunosorbent Assay, ELISA. III. Quantitation of Specific Antibodies by Enzyme-Labeled Anti-Immunoglobulin in Antigen-Coated Tubes," J. Immunology 109:129-135 (1972) (mistakenly referred to as Engval)                  |                |
|                                 | A92                   | Faure et al., "A Member of the Ste20/PAK Family of Protein Kinases is Involved in Both Arrest of Xenopus Oocytes at G2/Prophase of the First Meiotic Cell Cycle and in prevention of Apoptosis," EMBO J. 16:5550-61 (1997)                                     |                |
|                                 | A93                   | Felgner and Felgner, "Cationic Liposome-Mediated Transfection," Nature 337:387-388 (1989)  |                |
|                                 | A94                   | Felgner et al., "Lipofection: A Highly Efficient, Lipid-mediated DNA-transfection Procedure," Proc. Natl. Acad. Sci. USA 84:7413-7417 (1987)   |                |
|                                 | A95                   | Fernandes et al., "Biochemical and Antitumor Effects of 5,8-Dideazaisopteroylglutamate, a Unique Quinazoline Inhibitor of Thymidylate Synthase," Cancer Research 43:1117-1123 (1983)   |                |
|                                 | A96                   | Ferris et al., "Synthesis of Quinazoline Nucleosides from Ribose and Anthranilonitrile. Application of Phase-Transfer Catalysis in Nucleoside Synthesis," J. Org. Chem. 44(2):173-178 (1979)   |                |

|                    |  |                 |  |
|--------------------|--|-----------------|--|
| Examiner Signature |  | Date Considered |  |
|--------------------|--|-----------------|--|

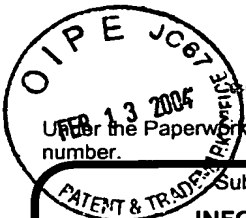
\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.





Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

Date Submitted: February 13, 2004

(use as many sheets as necessary)

**Complete if Known**

|                        |                 |
|------------------------|-----------------|
| Application Number     | Unassigned      |
| Filing Date            | 12/02/2003      |
| First Named Inventor   | Gregory Plowman |
| Group Art Unit         | 1652            |
| Examiner Name          | Unassigned      |
| Attorney Docket Number | 034536-0688     |

Sheet 7 of 15

**NON PATENT LITERATURE DOCUMENTS**

| Examiner Initials* | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>6</sup> |
|--------------------|-----------------------|--|----------------|
|                    | A97                   | Frost et al., "Cross-Cascade Activation of ERKs and Ternary Complex Factors by Rho Family Proteins," <u>EMBO J.</u> 16:6426-6438 (1997)  |                |
|                    | A98                   | Frost et al., "Differential Effects of PAK1-activating Mutations Reveal Activity-dependent and -independent Effects on Cytoskeletal Regulation," <u>J. Biol. Chem.</u> 273:28191-28198 (1998)  |                |
|                    | A99                   | Fry et al., "A Specific Inhibitor of the Epidermal Growth Factor Receptor Tyrosine Kinase," <u>Science</u> 265:1093-1095 (1994)  |                |
|                    | A100                  | Galisteo et al., "The Adaptor Protein Nck Links Receptor Tyrosine Kinases with the Serine-Threonine Kinase Pak1," <u>J. Biol. Chem.</u> 271:20997-21000 (1996)   |                |
|                    | A101                  | Gazit et al., "Tyrphostins 1. Synthesis and Biological Activity of Protein Tyrosine Kinase Inhibitors," <u>J. Med. Chem.</u> 32:2344-2352 (1989)   |                |
|                    | A102                  | Gazit et al., "Tyrphostins. 3. Structure-Activity Relationship Studies of a $\alpha$ -Substituted Benzylidenemalononitrile 5-S-Aryltyrphostins," <u>J. Med. Chem.</u> 36:3556-3564 (1993)  |                |
|                    | A103                  | GenBank Accession Number AAD01210. serine/threonine kinase [homo sapiens]. Melnick MB. Publicly available January 5, 1999.   |                |
|                    | A104                  | Gerard et al., "cDNA Synthesis by Cloned Moloney Murine Leukemia Virus Reverse Transcriptase Lacking Rnase H Activity," <u>Focus</u> 11(4):66-69 (1989)  |                |
|                    | A105                  | Gilman et al., "Isolation of sigma-28-specific promoters from Bacillus subtilis DNA," <u>Gene</u> 32:11-20(1984)   |                |
|                    | A106                  | Glick and Whitney, "Factors affecting the expression of foreign proteins in Escherichia coli," <u>Journal of Industrial Microbiology</u> 1:277-282 (1987)  |                |
|                    | A107                  | Goding, "Conjugation of Antibodies with Fluorochromes: Modifications to the Standard Methods," <u>J. Immunological Methods</u> 13:215-226 (1976)   |                |
|                    | A108                  | Gold et al., "Translational Initiation in Prokaryotes." <u>Ann. Rev. Microbiol.</u> 35:365-403 (1981)  |                |
|                    | A109                  | Gottesman, "Bacterial Regulation: Global Regulatory Networks," <u>Ann. Rev. Genet.</u> 18:415-441 (1984)   |                |
|                    | A110                  | Gryczan, "Ch. 10 - Molecular Cloning in Bacillus subtilis," in <u>The Molecular Biology of the Bacilli</u> , edited by Dubnau, Academic Press, New York, pp. 307-329 (1982)  |                |

Examiner  
Signature

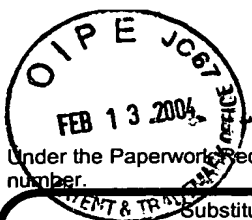
Date  
Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

MODIFIED PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

Date Submitted: February 13, 2004

(use as many sheets as necessary)

**Complete if Known**

|                        |                 |
|------------------------|-----------------|
| Application Number     | Unassigned      |
| Filing Date            | 12/02/2003      |
| First Named Inventor   | Gregory Plowman |
| Group Art Unit         | 1652            |
| Examiner Name          | Unassigned      |
| Attorney Docket Number | 034536-0688     |

Sheet 8 of 15

**NON PATENT LITERATURE DOCUMENTS**

| Examiner Initials* | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.                 | T <sup>6</sup> |
|--------------------|-----------------------|--|----------------|
|                    | A111                  | Hamer and Walling, "Regulation In Vivo of a Cloned Mammalian Gene: Cadmium Induces the Transcription of a Mouse Metallothionein Gene in SV40 Vectors," <u>J. of Molecular and Applied Genetics</u> 1:273-288 (1982) (also referred to as Hammer)                               |                |
|                    | A112                  | Hammer et al., "Spontaneous Inflammatory Disease in Transgenic Rats Expressing HLA-B27 and Human $\beta_2m$ : An Animal Model of HLA-B27-Associated Human Disorders," <u>Cell</u> 63:1099-1112(1990)   |                |
|                    | A113                  | Hirst et al., "Predicting Leucine Zipper Structures From Sequence," <u>Protein Engineering</u> 9:657-662 (1996)  |                |
|                    | A114                  | Houdebine and Chourrout, "Transgenesis in Fish," <u>Experientia</u> 47:891-897 (1991)  |                |
|                    | A115                  | Hu et al., "Human HPK1, a Novel Human Hematopoietic Progenitor Kinase that Activates the JNK/SAPK Kinase Cascade," <u>Genes and Dev.</u> 10:2251-2264 (1996)   |                |
|                    | A116                  | Hurby et al., in <u>Synthetic Peptides: A User's Guide</u> , edited by Grant, Washington University School of Medicine, W.H. Freeman and Company, New York, pp. 289-307 (1992)   |                |
|                    | A117                  | Hutchison M., "Isolation Of TAO1, A Protein Kinase That Activates MEKs In Stress-Activated Protein Kinase Cascades", <u>Journal Of Biological Chemistry</u> , US, American Society Of Biological Chemists, Baltimore, MD, Vol. 273, No. 44, Pages 28625-28632, 30 October 1998 |                |
|                    | A118                  | Innis et al., <u>PCR Protocols: A Guide to Methods and Applications</u> , edited by Michael A. Innis et al., Academic Press, San Diego (1990) (TABLE OF CONTENTS ONLY)   |                |
|                    | A119                  | Izaki, <u>Japanese Journal of Bacteriology</u> 33(6):729-742 (1978)  |                |
|                    | A120                  | Jackman et al., "ICI D1694, a Quinazoline Antifolate Thymidylate Synthase Inhibitor That Is a Potent Inhibitor of L1210 Tumor Cell Growth in Vitro and in Vivo: A New Agent for Clinical Study," <u>Cancer Research</u> 51:5579-5586 (1991)                                    |                |
|                    | A121                  | Jasny, "Insect Viruses Invade Biotechnology," <u>Science</u> 238:1653 (1987)   |                |
|                    | A122                  | John and Twitty, "Plasmids as Epidemiologic Markers in Nosocomial Gram-Negative Bacilli: Experience at a University and Review of the Literature," <u>Reviews of Infectious Diseases</u> 8:693-704 (1986)  |                |
|                    | A123                  | Johnston and Hopper, "Isolation of the yeast regulatory gene GAL4 and analysis of its dosage effects on the galactose/melibiose regulon," <u>Proc. Natl. Acad. Sci. USA</u> 79:6971-6975 (1982)  |                |
|                    | A124                  | Jones et al., "Quinazoline Antifolates Inhibiting Thymidylate Synthase: Variation of the Amino Acid," <u>J. Med. Chem.</u> 29:1114-1118(1986)  |                |

Examiner  
Signature

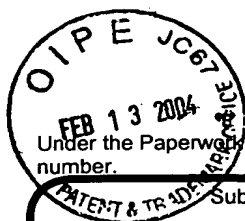
Date  
Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

MODIFIED PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

Date Submitted: February 13, 2004

(use as many sheets as necessary)

**Complete if Known**

|                        |                 |
|------------------------|-----------------|
| Application Number     | Unassigned      |
| Filing Date            | 12/02/2003      |
| First Named Inventor   | Gregory Plowman |
| Group Art Unit         | 1652            |
| Examiner Name          | Unassigned      |
| Attorney Docket Number | 034536-0688     |

Sheet 9 of 15

**NON PATENT LITERATURE DOCUMENTS**

| Examiner Initials* | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>6</sup> |
|--------------------|-----------------------|--|----------------|
|                    | A125                  | Joyner et al., "Production of a mutation in mouse En-2 gene by homologous recombination in embryonic stem cells," <u>Nature</u> 338:153-156 (1989)   |                |
|                    | A126                  | Kasprzak et al., "Location of a Contact Site Between Actin and Myosin in the Three-Dimensional Structure of the Acto-S1 Complex," <u>Biochemistry</u> 28:9230-9238 (1989)  |                |
|                    | A127                  | Kaur et al., "Tyrphostin induced growth inhibition: correlation with effect on p210 <sup>bcr-abl</sup> autokinase activity in K562 chronic myelogenous leukemia," <u>Anti-Cancer Drugs</u> 5:213-222 (1994)  |                |
|                    | A128                  | Kendall and Cohen, "Plasmid Transfer in Streptomyces lividans: Identification of a kil-kor System Associated with the Transfer Region of PIJ101," <u>Journal of Bacteriology</u> 169:4177-4183 (1987)  |                |
|                    | A129                  | Kiefer et al., "HPK1, a Hematopoietic Protein Kinase Activating the SAPK/JNK Pathway," <u>EMBO J.</u> 15:7013-7025 (1996)  |                |
|                    | A130                  | King et al., "Site-specific dephosphorylation and deactivation of the human insulin receptor tyrosine kinase by particulate and soluble phosphotyrosyl protein phosphatases," <u>Biochem. J.</u> 275:413-418 (1991)  |                |
|                    | A131                  | King et al., "The Protein Kinase Pak3 Positively Regulates Raf-1 Activity Through Phosphorylation of Serine 338," <u>Nature</u> 396:180-183 (1998)   |                |
|                    | A132                  | Knaus et al., "Regulation of Human Leukocyte p21-Activated Kinases Through G Protein-Coupled Receptors," <u>Science</u> 269:221-223 (1995)   |                |
|                    | A133                  | Knuutila et al., "DNA Copy Number Amplifications in Human Neoplasms: Review of Comparative Genomic Hybridization Studies," <u>Am. J. Pathol</u> 152:1107-1123(1998)  |                |
|                    | A134                  | Kohler and Milstein, "Continuous cultures of fused cells secreting antibody of predefined specificity," <u>Nature</u> 256:495-497 (1975)   |                |
|                    | A135                  | Kozak, "An analysis of 5'-noncoding sequences from 699 vertebrate messenger RNAs," <u>Nucleic Acids Research</u> 15:8125-8148 (1987)   |                |
|                    | A136                  | Kumar et al., "Novel Homologues of CSBP/p38 MAP Kinase: Activation, Substrate Specificity and Sensitivity to Inhibition by Pyridinyl Imidazoles," <u>Biochem. Biophys. Res. Commun.</u> 235:533-528 (1997)   |                |
|                    | A137                  | Kuo et al., "Effects of signalling transduction modulators on the transformed phenotypes in v-H-ras-transformed NIH 3T3 cells," <u>Cancer Letters</u> 74:197-202 (1993)  |                |
|                    | A138                  | Kuramochi et al., "LOK Is A Novel Mouse STE20-like Protein Kinase That Is Expressed Predominantly In Lymphocytes", The Journal Of Biological Chemistry, Vol. 272, No. 36, Pages 22679-22684, 5 September 1997  |                |

Examiner  
Signature

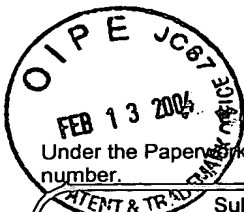
Date  
Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

MODIFIED PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

Date Submitted: February 13, 2004

(use as many sheets as necessary)

Sheet 10 of 15

**Complete if Known**

|                        |                 |
|------------------------|-----------------|
| Application Number     | Unassigned      |
| Filing Date            | 12/02/2003      |
| First Named Inventor   | Gregory Plowman |
| Group Art Unit         | 1652            |
| Examiner Name          | Unassigned      |
| Attorney Docket Number | 034536-0688     |

**NON PATENT LITERATURE DOCUMENTS**

| Examiner Initials* | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>6</sup> |
|--------------------|-----------------------|--|----------------|
|                    | A139                  | Lee and Skibo, "Active-Site-Directed Reductive Alkylation of Xanthine Oxidase by Imidazo[4,5-g]quinazoline-4,9-diones Functionalized with a Leaving Group," <u>Biochemistry</u> 26:7355-7362 (1987)  |                |
|                    | A140                  | Leeuw et al., "interaction of a G-protein $\beta$ -subunit with a Conserved Sequence in Ste20/PAK Family Protein Kinases," <u>Nature</u> 391:191-195 (1998)  |                |
|                    | A141                  | Lemus et al., "Studies of Extended Quinone Methides. Synthesis and Physical Studies of Purine-like Monofunctional and Bifunctional Imidazo[4,5-g]quinazoline Reductive Alkylating Agents," <u>J. Org. Chem.</u> 54:3611-3618 (1989)                            |                |
|                    | A142                  | Levitzki, "Tyrphostins: tyrosine kinase blockers as novel antiproliferative agents and dissectors of signal transduction," <u>FASEB J.</u> 6:3275-3282 (1992)  |                |
|                    | A143                  | Ley and Seng, "Synthesis Using Benzofuroxan," <u>Synthesis</u> 1975:415-422 (1975)   |                |
|                    | A144                  | Lu et al., "CDC42 and Rac1 are implicated in the Activation of the Nef-associated Kinase and Replication of HIV-1," <u>Current Biology</u> 6:1677-1684 (1996)  |                |
|                    | A145                  | Lui et al., "A Drosophila TNF-receptor-associated Factor (TRAF) Binds the Ste20 Kinase Misshapen and Activates Jun Kinase," <u>Curr. Biol.</u> 9:101-104 (1999)  |                |
|                    | A146                  | Lupas et al., "Predicting Coiled Coils from Protein Sequences," <u>Science</u> 252:1162-1164(1991)   |                |
|                    | A147                  | Lupas, "Prediction and Analysis of Coiled-Coil Structures," <u>Meth. Enzymology</u> 266:513-525 (1996)   |                |
|                    | A148                  | Lutz et al., "The Distribution of Two hnRNP-Associated Proteins Defined by a Monoclonal Antibody Is Altered in Heat-Shocked HeLa Cells," <u>Experimental Cell Research</u> 175:109-124 (1988)  |                |
|                    | A149                  | Lyll et al., "Tyrphostins Inhibit Epidermal Growth Factor (EGF)-Receptor Tyrosine Kinase Activity in Living Cells and EGF-stimulated Cell Proliferation," <u>J. Biol. Chem.</u> 264:14503-14509 (1989)   |                |
|                    | A150                  | Madaule et al., "A Novel Partner for the (FTP-bound Forms of rho and rac," <u>FEBS Letters</u> 377:243-238 (1995)  |                |
|                    | A151                  | MaGuire et al., "A New Series of PDGF Receptor Tyrosine Kinase Inhibitors: 3-Substituted Quinoline Derivatives," <u>J. Med. Chem.</u> 37:2129-2137 (1994)  |                |
|                    | A152                  | Maniatis, "Ch. 11 - Recombinant DNA Procedures in the Study of Eukaryotic Genes," in <u>Cell Biology: A Comprehensive Treatise, Volume 3. Gene Sequence Expression</u> , Academic Press, NY, pp. 563-608 (1980)  |                |

Examiner  
Signature

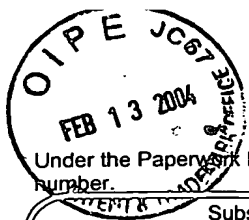
Date  
Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

|   |  |                          |                 |
|---|--|--------------------------|-----------------|
| Substitute for form 1449B/PTO<br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br>Date Submitted: February 13, 2004<br>(use as many sheets as necessary) |  | <b>Complete if Known</b> |                 |
|   |  | Application Number       | Unassigned      |
| Sheet 11 of 15  |  | Filing Date              | 12/02/2003      |
|   |  | First Named Inventor     | Gregory Plowman |
|   |  | Group Art Unit           | 1652            |
|   |  | Examiner Name            | Unassigned      |
|   |  | Attorney Docket Number   | 034536-0688     |

| NON PATENT LITERATURE DOCUMENTS |                       |  |                |
|---------------------------------|-----------------------|--|----------------|
| *Examiner Initials*             | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.                 | T <sup>6</sup> |
|                                 | A153                  | Manser et al., "A Brain Serine/Threonine Protein Kinase Activated by Cdc42 and Rac1," <u>Nature</u> 367:40-46 (1994)   |                |
|                                 | A154                  | Manser et al., "PAK Kinases are Directly Coupled to the PIX Family of Nucleotide Exchange Factors," <u>Mol. Cell</u> 1:183-192 (1998)  |                |
|                                 | A155                  | Mark et al., "Instability of Dinucleotide Repeats in Hodgkin's Disease," <u>Am. J. Hematol.</u> 57:148-152 (1998)  |                |
|                                 | A156                  | Maxwell et al., " <sup>19</sup> F Nuclear Magnetic Resonance Imaging of Drug Distribution in Vivo: The Diposition of an Antifolate Anticancer Drug in Mice," <u>Magnetic Resonance in Medicine</u> 17:189-196 (1991)   |                |
|                                 | A157                  | McKnight, "Functional Relationships between Transcriptional Control Signals of the Thymidine Kinase Gene of Herpes Simplex Virus," <u>Cell</u> 31:355-365 (1982)   |                |
|                                 | A158                  | Miller et al., "An Insect Baculovirus Host-Vector System for High-Level Expression of Foreign Genes," in <u>Genetic Engineering: Principles and Methods</u> , edited by Setlow et al., Plenum Press, 8:277-298 (1986)  |                |
|                                 | A159                  | Miller, "Human gene therapy comes of age," <u>Nature</u> 357:455-460 (1992)  |                |
|                                 | A160                  | Mini et al., "Cytotoxic Effects of Folate Antagonists against Methotrexate-resistant Human Leukemic Lymphoblast CCRF-CEM Cell Lines," <u>Cancer Research</u> 45:325-330 (1985)   |                |
|                                 | A161                  | Nelson et al., "Detection of Acridinium Esters by Chemiluminescence," <u>Nonisotopic DNA Probe Techniques</u> , ed. Larry J. Kricka, (San Diego: Academic Press, Inc.) pp. 275-310 (1992)  |                |
|                                 | A162                  | Nikolic et al., "The p35/Cdk5 Kinase is a Neuron-Specific Rac Effector that Inhibits Paki Activity," <u>Nature</u> 395:194-198 (1998)  |                |
|                                 | A163                  | Okayama and Berg, "A cDNA Cloning Vector That Permits Expression of cDNA Inserts in Mammalian Cells," <u>Molecular and Cellular Biology</u> 3:280-289(1983)  |                |
|                                 | A164                  | Osada et al., "A Domain Containing the Cdc42/Rac Interactive Binding (CRIB) Region of p65 PAK Inhibits Transcriptional Activation and Cell Tranformation Mediated by the Ras-Rac Pathway," <u>FEBS Letters</u> 404:227-233 (1997).   |                |
|                                 | A165                  | Peterson and Barnes, "Genistein and Biochanin A Inhibit the Growth of Human Prostate Cancer Cells but not Epidermal Growth Factor Receptor Tyrosine Autophosphorylation," <u>The Prostate</u> 22:335-345 (1993)  |                |
|                                 | A166                  | Phillips and Castle, "Quino[1,2-c]quinazolines. I. Synthesis of Quino[1,2-c]quinazolinium Derivatives and the Related Indazolo[2,3-a]quinoline Derivatives as Analogs of the Antitumor Benzo[c]phenanthridine Alkaloids," <u>J. Heterocyclic Chemistry</u> 17:1489-1496 (1980) |                |

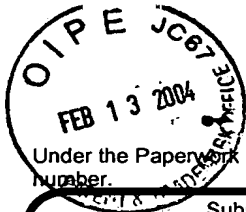
|                    |                 |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

MODIFIED PTO/SB/08 (08-00)  
Approved for use through 10/31/2002. OMB 0651-0031  
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

|  |    |                          |                 |                        |             |
|--|----|--------------------------|-----------------|------------------------|-------------|
| Substitute for form 1449B/PTO  |    | <b>Complete if Known</b> |                 |                        |             |
| <b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><br>Date Submitted: February 13, 2004<br><br>(use as many sheets as necessary) |    | Application Number       | Unassigned      |                        |             |
|  |    | Filing Date              | 12/02/2003      |                        |             |
|  |    | First Named Inventor     | Gregory Plowman |                        |             |
|  |    | Group Art Unit           | 1652            |                        |             |
|  |    | Examiner Name            | Unassigned      |                        |             |
| Sheet  | 12 | of                       | 15              | Attorney Docket Number | 034536-0688 |

| NON PATENT LITERATURE DOCUMENTS |                       |  |                |
|---------------------------------|-----------------------|--|----------------|
| *Examiner Initials*             | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>6</sup> |
|                                 | A167                  | Pillemer et al., "Insulin Dependence of Murine Lymphoid T-Cell Leukemia," <u>Brit. J. Cancer</u> 50:80-85 (1992)   |                |
|                                 | A168                  | Pombo et al., "Activation of a Human Ste20-like Kinase by Oxidant Stress Defines a Novel Response Pathway," <u>EMBO J.</u> 17:4537-4546 (1996)   |                |
|                                 | A169                  | Pombo et al., "Activation of the SAPK Pathway by the Human STE20 Homologue Germinal Centre Kinase," <u>Nature</u> 377:750-754 (1995)   |                |
|                                 | A170                  | Pombo et al., "Activation of the Ste20-like Oxidant Stress Response Kinase-1 During the Initial Stages of Chemical Anoxia-induced Necrotic Cell Death," <u>J. Biol. Chem.</u> 272:29372-29379 (1997)   |                |
|                                 | A171                  | Posner et al., "Kinetics of Inhibition by Tyrphostins of the Tyrosine Kinase Activity of the Epidermal Growth Factor Receptor and Analysis by a New Computer Program," <u>Molecular Pharmacology</u> 45:673-683 (1993)   |                |
|                                 | A172                  | Pursel et al., "Genetic Engineering of Livestock," <u>Science</u> 244: 1281-1288 (1989)  |                |
|                                 | A173                  | Qian et al., "Purification and Cloning of a Protein Kinase that Phosphorylates and Activates the Polo-Like Kinase Plx1," <u>Science</u> 282:1701-1704 (1998)   |                |
|                                 | A174                  | Qian et al., "Dominant-negative Zeta-associated Protein 70 Inhibits T Cell Antigen Receptor Signaling," <u>J. Exp. Med.</u> 183:611-620 (1996)   |                |
|                                 | A175                  | Reece et al., "Pharmacokinetics of Trimetrexate Administered by Five-Day Continuous Infusion to Patients with Advanced Cancer," <u>Cancer Research</u> 47:2996-2999 (1987)   |                |
|                                 | A176                  | Ren et al., "In its Active Form, the GTP-Binding Protein rab8 Interacts with a Stress-Activated Protein Kinase," <u>Proc. Natl. Acad. Sci.</u> 93:5151-5155 (1996)   |                |
|                                 | A177                  | Rendu et al., "Inhibition of Platelet Activation by Tyrosine Kinase Inhibitors," <u>Biochemical Pharmacology</u> 44(5):881-888 (1992)  |                |
|                                 | A178                  | Robertson, <u>Teratocarcinomas and embryonic stem cells: a practical approach</u> , IRL Press (1987) (TABLE OF CONTENTS)   |                |
|                                 | A179                  | Roe et al., "TOUSLED Is a Nuclear Serine/Threonine Protein Kinase that Requires a Coiled-coil Region for Oligomerization and Catalytic Activity," <u>J. Biol. Chem.</u> 272:5838-5845 (1997)   |                |
|                                 | A180                  | Rubin, "Drosophila melanogaster as an Experimental Organism," <u>Science</u> 240:1453-1459 (1988)  |                |
|                                 | A181                  | Rudel and Bokoch, "Membrane and Morphological Changes in Apoptotic Cells Regulated by Caspase-Mediated Activation of Pak2," <u>Science</u> 276:1571-4 (1997)   |                |

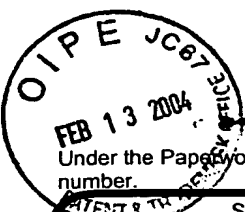
|                    |  |                 |  |
|--------------------|--|-----------------|--|
| Examiner Signature |  | Date Considered |  |
|--------------------|--|-----------------|--|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

Date Submitted: February 13, 2004

(use as many sheets as necessary)

**Complete if Known**

|                        |                 |
|------------------------|-----------------|
| Application Number     | Unassigned      |
| Filing Date            | 12/02/2003      |
| First Named Inventor   | Gregory Plowman |
| Group Art Unit         | 1652            |
| Examiner Name          | Unassigned      |
| Attorney Docket Number | 034536-0688     |

Sheet 13 of 15

**NON PATENT LITERATURE DOCUMENTS**

| Examiner Initials* | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.  | T <sup>6</sup> |
|--------------------|-----------------------|---|----------------|
|                    | A182                  | Sambrook, Maniatis and Fritsch, <u>Molecular Cloning: A Laboratory Manual. 2<sup>nd</sup> Edition</u> , Cold Spring Harbor Laboratory Press (1989) (TABLE OF CONTENTS - ALL THREE VOLUMES)  |                |
|                    | A183                  | Sauro and Thomas, "Decreased Sensitivity of Aorta from Hypertensive Rats to Vasorelaxation by Tyrphostin," <u>Life Sciences</u> 53:PL371-376 (1993)   |                |
|                    | A184                  | Sauro and Thomas, "Tyrphostin Attenuates Platelet-Derived Growth Factor-Induced Contraction in Aortic Smooth Muscle Through Inhibition of Protein Tyrosine Kinase(s)," <u>The Journal of Pharmacology and Experimental Therapeutics</u> 267:1119-1125 (1993)  |                |
|                    | A185                  | Schinkmann and Blenis, "Cloning and Characterization of a Human STE20-like Protein Kinase with Unusual Cofactor Requirements," <u>J. Biol. Chem.</u> 272:28695-28703 (1997)   |                |
|                    | A186                  | Schlesinger et al., "The Tao of MEKK," <u>Frontiers in Bioscience</u> 3:D1181-6 (1998)  |                |
|                    | A187                  | Sculier et al., "Role of an Intensive Care Unit (ICU) in a Medical Oncology Department," <u>Cancer Immunol. and Immunotherapy</u> 23:A65 at abstract no. 257 (1986)   |                |
|                    | A188                  | Shi and Kehrl, "Activation of Stress-activated Protein Kinase/c-Jun N-terminal Kinase, but Not NF- $\kappa$ B, by the Tumor Necrosis Factor (TNF) Receptor 1 Through a TNF Receptor-associated Factor 2- and Germinal Center Kinase Related-dependent Pathway," <u>J. Biol. Chem.</u> 272:32102-32107 (1997)        |                |
|                    | A189                  | Sikora and Grzelakowska-Sztabert, "Quinazoline CB 3717 and CB 3703 Inhibitors of Folate Retention and Metabolism in Ehrlich Ascites Carcinoma Cells and Some Organs of the Host-Mouse," <u>Cancer Letters</u> 23:289-295 (1984)   |                |
|                    | A190                  | Sikora et al., "Development of an Assay for the Estimation of N <sup>10</sup> -Propargyl-5,8-dideazafolic Acid Polyglutamates in Tumor Cells," <u>Analytical Biochemistry</u> 172:344-355 (1988)  |                |
|                    | A191                  | Silver et al., "Amino terminus of the yeast GAL4 gene product is sufficient for nuclear localization," <u>Proc. Natl. Acad. Sci. USA</u> 81:5951-5955 (1984)  |                |
|                    | A192                  | Simons et al., "Gene Transfer into Sheep," <u>Bio/Technology</u> 6:179-182 (1988) (also referred to as Simms or Simmons)  |                |
|                    | A193                  | Smith and Waterman, "Identification of Common Molecular Subsequences," <u>J. Mol. Biol.</u> 147:195-197 (1981)  |                |
|                    | A194                  | St. Groth and Scheidegger, "Production of Monoclonal Antibodies: Strategy and Tactics," <u>J. Immunol. Methods</u> 35:1-21 (1980)   |                |
|                    | A195                  | Stemberger et al., "The Unlabeled Antibody Enzyme Method of Immunohistochemistry: Preparation and Properties of Soluble Antigen-Antibody Complex (Horseradish Peroxidase-Antihorseradish Peroxidase) and its Use in Identification of Spirochetes," <u>J. Histochemistry and Cytochemistry</u> 18(5):315-333 (1970) |                |

Examiner  
Signature

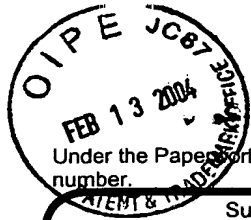
Date  
Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

MODIFIED PTO/SB/08 (08-00)  
Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

Date Submitted: February 13, 2004

(use as many sheets as necessary)

**Complete if Known**

|                        |                 |
|------------------------|-----------------|
| Application Number     | Unassigned      |
| Filing Date            | 12/02/2003      |
| First Named Inventor   | Gregory Plowman |
| Group Art Unit         | 1652            |
| Examiner Name          | Unassigned      |
| Attorney Docket Number | 034536-0688     |

Sheet 14 of 15

**NON PATENT LITERATURE DOCUMENTS**

| Examiner Initials* | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.  | T <sup>6</sup> |
|--------------------|-----------------------|---|----------------|
|                    | A196                  | Su et al., "NIK Is A New Ste20-Related Kinase That Binds NCK and MEKK1 and Activates The SAPK/JNK Cascade Via A Conserved Regulatory Domain", The EMBO Journal, Vol. 16, No. 6, Pages 1279-1290, 1997   |                |
|                    | A197                  | Su et al., "The Drosophila Ste20-related Kinase Misshapen is Required for Embryonic Dorsal Closure and Acts Through a JNK MAPK Module on an Evolutionarily Conserved Signaling Pathway," <u>Genes Dev.</u> 12:2371-2380 (1998)  |                |
|                    | A198                  | Su et al., "NIK is a New Ste20-related Kinase that Binds NCK and MEKK1 and Activates the SAPK/JNK Cascade via a Conserved Regulatory Domain," <u>EMBO J.</u> 16:1279-1290 (1997)  |                |
|                    | A199                  | Sudol, "Structure and Function of the WW Domain," <u>Prog. Biochys. Mol. Bio.</u> 65:113-132 (1996)   |                |
|                    | A200                  | Swanek et al., "Jun N-Terminal Kinase/Stress-Activated Protein Kinase (JNK/SAPK) Is Required for Lipopolysaccharide Stimulation of Tumor Necrosis Factor Alpha (TNF- $\alpha$ ) Translation: Glucocorticoids Inhibit TNF- $\alpha$ Translation by Blocking JNK/SAPK," <u>Mol. Cell. Biol.</u> 6274-6282 (1997)                |                |
|                    | A201                  | Szczepanowska et al., "Identification by Mass Spectrometry of the Phosphorylated Residue Responsible for Activation of the Catalytic Domain of Myosin I Heavy Chain Kinase, A Member of the PAK/STE20 Family," <u>Proc. Natl. Acad. Sci.</u> 94:8503-8508 (1997)  |                |
|                    | A202                  | Tang et al., "Kinase-Deficient Pak1 Mutants Inhibit Ras Transformation of Rat-1 Fibroblasts," <u>Mol. Cell. Biol.</u> 17:4454-4464 (1997)   |                |
|                    | A203                  | Tijssen, <u>Practice and Theory of Enzyme Immunoassays: Laboratory Techniques in Biochemistry and Molecular Biology</u> , Volume 15, Elsevier Science Publishers, Amsterdam, The Netherlands (1985) (TABLE OF CONTENTS ONLY)  |                |
|                    | A204                  | Treisman et al., "Misshapen Encodes a Protein Kinase Involved in Cell Shape Control in Drosophila," <u>Gene</u> 186:119-125 (1997)  |                |
|                    | A205                  | Ulmanen et al., "Transcription and Translation of Foreign Genes in Bacillus subtilis by the Aid of a Secretion Vector," <u>Journal of Bacteriology</u> 162:176-182 (1985)   |                |
|                    | A206                  | VanArsdale and Ware, "TNF Receptor Signal Transduction," <u>J. Immunol.</u> 153:3043-3050 (1994)  |                |
|                    | A207                  | Wang et al., "Activation of the Hematopoietic Progenitor Kinase-1 (HPK1)-dependent, Stress-activated c-Jun N-terminal Kinase (JNK) Pathway by Transforming Growth Factor $\beta$ (TGF- $\beta$ )-activated Kinase (TAK1), a Kinase Mediator of TGF $\beta$ Signal Transduction," <u>J. Biol. Chem.</u> 272:22771-22775 (1997) |                |
|                    | A208                  | Ward et al., "Construction and characterisation of a series of multi-copy promoter-probe plasmid vectors for Streptomyces using the aminoglycoside phosphotransferase gene from Tn5 as indicator," <u>Mol. Gen. Genet.</u> 203:468-478 (1986)   |                |
|                    | A209                  | Wilchek and Jakoby, "The Literature on Affinity Chromatography," <u>Methods in Enzymology</u> 34:3-10 (1974) (also referred to as Jacoby)   |                |

Examiner  
Signature

Date  
Considered

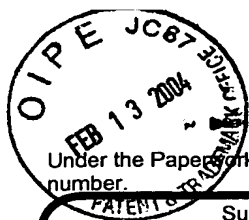
\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.





Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

MODIFIED PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

Date Submitted: February 13, 2004

(use as many sheets as necessary)

Sheet 15 of 15

**Complete if Known**

|                        |                 |
|------------------------|-----------------|
| Application Number     | Unassigned      |
| Filing Date            | 12/02/2003      |
| First Named Inventor   | Gregory Plowman |
| Group Art Unit         | 1652            |
| Examiner Name          | Unassigned      |
| Attorney Docket Number | 034536-0688     |

**NON PATENT LITERATURE DOCUMENTS**

| Examiner Initials* | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T <sup>6</sup> |
|--------------------|-----------------------|--|----------------|
|                    | A210                  | Wolbring et al., "Inhibition of GTP-utilizing Enzymes by Tyrphostins," <u>J. Biol. Chem.</u> 269:22470-22472 (1994)  |                |
|                    | A211                  | Wu et al., "Molecular Characterization of Ste20p, a Potential Mitogea-activated protein or Extracellular Signal-regulated Kinase Kinase (MEK)Kinase Kinase from <i>Saccharomyces cerevisiae</i> ," <u>J. Biol. Chem.</u> 270:15984-15992 (1995)                |                |
|                    | A212                  | Xu et al., "Three-dimensional Structure of the Tyrosine Kinase c-Src," <u>Nature</u> 385:595-602 (1997)  |                |
|                    | A213                  | Yablonski et al., "A Nck-Pak1 Signaling Module is Required for T-cell Receptor-mediated Activation of NFAT, but not of JNK," <u>EMBO J.</u> 17:5647-5657 (1998)  |                |
|                    | A214                  | Yan et al., "Activation of Stress-activated Protein Kinase by MEKK1 Phosphorylation of its Activator SEK1," <u>Nature</u> 372:798-800(1994)  |                |
|                    | A215                  | Yanagisawa et al., "A Novel Serine/Threonine Kinase Gene, Gek 1, Is Expressed in Meiotic Testicular Germ Cells and Primordial Germ Cells," <u>Mol. Reprod. and Dev.</u> 45:411-420 (1996)  |                |
|                    | A216                  | Yang et al., "In Vivo and In Vitro Gene Transfer to Mammalian Somatic Cells by Particle Bombardment," <u>Proc. Natl. Acad. Sci. USA</u> 87:9568-9572 (1990)  |                |
|                    | A217                  | Yao et al., "A Novel Human STE20-Related Protein Kinase, HGK, That Specifically Activates the c-Jun N-terminal Kinase Signaling Pathway," <u>J. Biol. Chem.</u> 274:2118-25(1999)  |                |
|                    | A218                  | Yoneda et al., "The Antiproliferative Effects of Tyrosine Kinase Inhibitors Tyrphostins on a Human Squamous Cell Carcinoma in Vitro and in Nude Mice," <u>Cancer Research</u> 51:4430-4435 (1991)  |                |
|                    | A219                  | Yuan. "Transducing Signals of Life and Death," <u>Curr. Opinion in Cell. Biol.</u> 9:247-251 (1997)  |                |
|                    | A220                  | Zhang et al., "Rho Family GTPases Regulate p38 Mitogen-activated Protein Kinase Through the Downstream Mediator Pak1," <u>J. Biol. Chem.</u> 270:23934-23936 (1995)  |                |
|                    | A221                  | Zhu and Hedgecock, "Mig- 15 Encodes a Novel Ser/Thr Protein Kinase of the Ste-20/p65PAK Family," <u>Worm Breeder's Gazette</u> 14:76 (1997)  |                |

Examiner  
Signature

Date  
Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, PO Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450.